REMARKS

With the cancellation of claims 13, 31 and 34, claims 1-12, 25-28, 30, 32, 33 and 35-41 are pending.

Claims 13 and 31 have been cancelled as directed toward a non-elected invention.

Claim 34 has been cancelled as duplicative of claim 1 as amended above.

The insertion of "obtainable from *Pyrococcus furiosus, Pyrococcus kodakaraensis* KOD1 or *Thermococcus litoralis*" in claim 1 is supported by the specification at page 19, lines 15-18.

Claim 4 has been amended to make it independent of claim 1 as filed. Applicants submitted that the amendment to claim 4 would not narrow the scope of claim 4. Applicants would like to thank Examiner Hutson for holding that claims 4-12 would be allowed if made independent of a rejected base claim.

The replacement of "PCT" with "PCR" in claims 39-41 has been made to correct an obvious typographical error and should not narrow the scope of the amended recitations.

Applicant's Statement of Interview Summary

Applicant's representative would like to thank Examiner Hutson for a helpful and courteous personal interview conducted on February 2, 2005. In the interview, the undersigned stated that "PCT" would be replaced with "PCR" in claims 39-41 and the Examiner indicated that the replacement should rendered the indefiniteness rejection moot. The undersigned also stated that claim 4, which were objected to, would be made independent of the rejected claim 3. The undersigned and the Examiner discussed proposed amendments, supported by page 19 of the specification, to claim 1 that might over the lack of written description and lack of scope of enablement rejections under 35 U.S.C. 112, first paragraph.

Claim Rejections - 35 U.S.C. 112

(A) Written Description Rejection

Applicants respectfully traverse the written description requirement of claims 1-3, 25-28, 30 and 32-41. Applicants submit that the claimed invention was adequately described to a person skilled in the art in the specification. For instance, the subject matter of these claims are described the specification at pages 5-13, 19 and 20-24, as well as Examples 1-9. In particular, page 19, lines 15-18, of the specification discloses modified thermostable DNA polymerases having 3'-5' exonuclease activity, wherein the modification is directed toward thermostable DNA polymerases obtainable from *Pyrococcus furiosus, Pyrococcus kodakaraensis* KOD1 or *Thermococcus litoralis* having 3'-5' exonuclease activity and the $DX_1EX_2X_3X_4H$ sequence (D:

aspartic acid, E: glutamic acid, H: histidine, X_1, X_2, X_3 and X_4: any amino acid) within the exonuclease I region, and wherein the histidine residue in the $DX_1EX_2X_3X_4H$ sequence is replaced by another amino acid. According to page 2, lines 6-14, of the specification, the unmodified thermostable DNA polymerase from *Pyrococcus furiosus, Pyrococcus kodakaraensis* KOD1 or *Thermococcus litoralis* having 3'-5' exonuclease activity are known. In addition, Fig. 1 shows the $DX_1EX_2X_3X_4H$ sequence in these thermostable DNA polymerases.

The Office Action indicates that the instant application as filed failed to disclose additional representative species as encompassed by claim 1 as filed. With the amendment to claim 1, applicants submit that the specification has disclosed sufficient number of representative species as encompassed by claim 1.

Furthermore, the specification describes that the modified thermostable DNA polymerases have modified 3'-5' exonuclease activity and/or amplification efficiency. Page 20, line 19 to page 24, line 3 of the specification describes the effects of replacing histidine in the $DX_1EX_2X_3X_4H$ sequence with acidic, neutral or basic amino acids. For instance, replacement of H in the $DX_1EX_2X_3X_4H$ sequence with an acidic amino acid results in a thermostable DNA polymerase with reduced 3'-5' exonuclease activity and improved amplifying efficiency (e.g. page 20, line 19 to page 21, line 3, and page 21, lines 23 to page 22, line 4, of the specification). Replacement of H in the $DX_1EX_2X_3X_4H$ sequence with a neutral amino acid results in a thermostable DNA polymerase with improved amplifying efficiency (e.g. page 21, lines 4-12, page 22, line 13 to page 23, line 5, and page 23, lines 14-19, the specification). Replacement of H in the $DX_1EX_2X_3X_4H$ sequence with a basic amino acid results in a thermostable DNA polymerase with improved 3'-5' exonuclease activity and/or fidelity in DNA replication (e.g. page 21, lines 13-22, the specification). See also Figures 2-4. Thus, there is disclosure of the particular structure to function/activity relationship in the modified thermostable DNA polymerase according to the claims.

Applicants submit that the disclosure of the specification as filed shows that applicants had possession of the claimed invention.

Withdrawal of the rejection based on an alleged lack of written description is requested.

(B) Non-Enablement Rejection

Applicants respectfully traverse the non-enablement rejection of claims 1-3, 25-28, 30 and 32-41. Page 20, line 19 to page 24, line 3 of the specification discloses the particular structure to function/activity relationship in various species of the modified thermostable DNA polymerase according to the claims. Replacement of H in the $DX_1EX_2X_3X_4H$ sequence with an acidic amino acid results in a thermostable DNA polymerase with reduced 3'-5' exonuclease activity and improved amplifying efficiency (e.g. page 20, line 19 to page 21, line 3, and page

21, lines 23 to page 22, line 4, of the specification). Replacement of H in the $DX_1EX_2X_3X_4H$ sequence with a neutral amino acid results in a thermostable DNA polymerase with improved amplifying efficiency (e.g. page 21, lines 4-12, page 22, line 13 to page 23, line 5, and page 23, lines 14-19, the specification). Replacement of H in the $DX_1EX_2X_3X_4H$ sequence with a basic amino acid results in a thermostable DNA polymerase with improved 3'-5' exonuclease activity and/or fidelity in DNA replication (e.g. page 21, lines 13-22, the specification). See also Figures 2-4. Thus, there is disclosure of the particular structure to function/activity relationship in the modified thermostable DNA polymerase according to the claims. The disclosure of the particular structure to function/activity relationship in the specification shows that the effects of replacing the histidine residue in the thermostable DNA polymerase are not unpredictable. The scope of the claimed invention is not overly broad in light of the disclosure. The disclosure shows how thermostable DNA polymerases having an exonuclease region I can be modified by replacing histidine in the $DX_1EX_2X_3X_4H$ sequence of the exonuclease region I. The disclosure of the function/activity relationship provides ample guidance to a person skilled in the art how to practice the claimed invention. With the disclosure and the knowledge of the art, a person skilled in the art can practice the claimed invention without undue experimentation. Applicants respectfully disagree with the Office Action's assertion that only the claimed invention involving a thermostable DNA polymerase having SEQ ID NO:2 is enabled. The enabling disclosure is commensurate in scope with the claims. Withdrawal of the non-enablement rejection is requested.

Conclusion

In light of the above reasoning, applicants submit that the application is in a condition for allowance. A Notice of Allowance is believed in order.

In the event that this paper is deemed not timely, applicants petition for an appropriate extension of time. The petition fee, and any other fees that may be required in relation to the filing of this paper, can be charged to Deposit Account No. 11-0600, referencing Docket No. 10089/14.

Respectfully Submitted,
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